

Significant Association between Toll-like Receptors Gene Polymorphism and Post-Transplantational Diabetes Mellitus

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Background: Posttransplantation diabetes mellitus (PTDM) is a serious metabolic complication after renal transplantation. Activation of the innate immune system via toll-like receptors (TLRs) is implicated in the pathogenesis of insulin resistance and deficiency. Although the links of diabetes and dysregulated innate immune responses with TLR signaling pathway was reported, relatively no studies have investigated the associations of PTDM. In this study, we investigated whether single nucleotide polymorphisms (SNPs) in TLRs have any association with PTDM in renal transplant recipients.

Methods: A total of 305 patients who had received kidney transplants without previously diagnosed diabetes were included. We analyzed the association between the PTDM development and the 6 SNPs within two genes of TLR2, one gene of TLR4, three genes of TLR6.

Results: Of 305 patients, PTDM developed in 51 patients (16.6%). Patients in the PTDM group were older than those in the non-PTDM group (45.56 ± 1.28 vs. 38.28 ± 0.71 years). The percentage of steroid-treated acute rejection episodes and using tacrolimus were no significant different between the two groups. The patients with PTDM had significantly higher allele frequency compared to those without PTDM for the TLR2 rs3804099*T, TLR4 rs1927914*T, TLR6 rs3775073*A, TLR6 rs3821985*C, TLR6 rs1039559*C alleles. Of six SNPs, the rs1927914 of the TLR4 gene and the rs 1039559 of the TLR6 were significantly associated with the development of PTDM after adjust with age. When haplotype analysis was performed, the frequency of the GGT haplotype of TLR6 was significantly higher in the non-PTDM group compared to the PTDM group (χ^2 4.836, $p=0.0279$) The ACC haplotype of TLR6 was associated with increased PTDM risk in the codominant (χ^2 9.207, $p=0.0024$).

Conclusion: Our study demonstrates a significant association between SNPs of the TLR4 rs192791 and TLR6 rs1039559 and PTDM in kidney transplantation recipients groups. These data suggest that activation of the innate immune system and inflammation via TLR activation might have an essential role in the pathogenesis of PTDM in renal transplantation.

Key Words: 신이식, 유전자 다형성, 이식후 당뇨

Toll-like receptors, Polymorphism, Post-transplantational diabetes mellitus, Kidney Transplantation